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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/013,071	12/10/2001	Zhaoning Zhu	IN01174	1388

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SCHERING-PLOUGH CORPORATION
PATENT DEPARTMENT (K-6-1, 1990)
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EXAMINER

MONDESI, ROBERT B

ART UNIT

PAPER NUMBER

1653

DATE MAILED: 04/15/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/013,071	ZHU ET AL.	
	Examiner	Art Unit	
	Robert B Mondesi	1653	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☒ Responsive to communication(s) filed on 06 April 2004.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-94 is/are pending in the application.
- 4a) Of the above claim(s) 24-94 is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-23 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on _____ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some * c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.

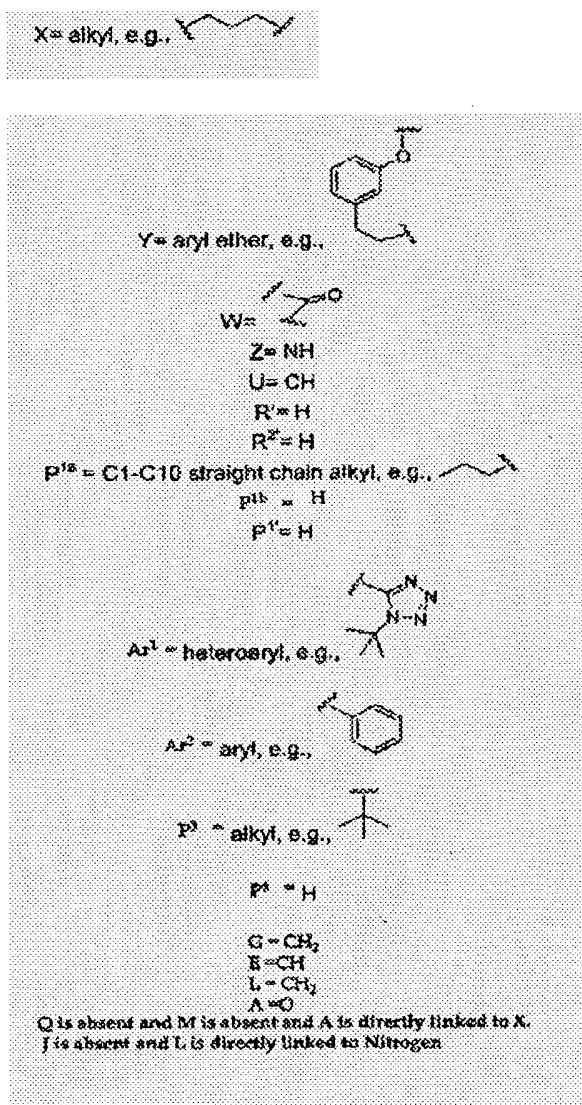
Attachment(s)

- | | |
|--|---|
| 1) <input type="checkbox"/> Notice of References Cited (PTO-892) | 4) <input type="checkbox"/> Interview Summary (PTO-413) |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____ |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date _____ | 6) <input type="checkbox"/> Other: _____ |

DETAILED ACTION

Response to restriction requirement

Applicant's election with traverse of Invention Group I, Claims 1-23, 28-54, 59-87 in amendment, with a further election of the a core structure in regards to the following moieties/atoms in reference to structure formula 1:



filed March 3, 2003 is acknowledged. The traversal is on the ground(s) that a complete search examination of claims with cause an undue burden and the examiner has not

established a clear reason in regards to separate classification, separate status in the and different field of search. This is not found persuasive because the applicant is reminded that there are possibly hundreds, if not thousands of compounds that are provided by the general structure formula of claim I, these compounds encompass a multitude of subclasses (514/357,255,311,307,471,332,340,365,253,424,422,399) and are varied not only in regards to structure but also in regards to activity- as it is demonstrated by the K_i value of compounds in Table A (for example compound I has a K_i activity value that is between 10,000nM and 50,000nM and compound XXI has a K_i activity value that is between 10nM and 99nm).

Therefore the requirement is still deemed proper and is made FINAL. **Claims 24-94** are withdrawn from further consideration by the Examiner because these Claims are drawn to non-elected inventions. **Claims 1-94** are pending in this application.

Priority

Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

If applicant desires priority under 35 U.S.C. 119(e) based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the

filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Information Disclosure Statement

The information disclosure sheets (IDS)s filed April 25, 2002 and June 09, 2003 have been received and are signed and considered, a copy of the IDS is attached to the following document.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-23 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for macrocyclic compounds 26 and 27 in table A (pages 113) and in the specification examples 19-23 (pages 92-105), does not reasonably provide enablement for all the compounds presented by the general structure formula (I) of claim 1. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to use or make the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized in *re Wands* 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir.1988). The court in *Wands* states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.'" (*Wands*, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (*Wands*, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the breadth of the claims, (2) the nature of the invention, (3) the state of the prior art, (4) the relative skill of those in the art, (5) the predictability or unpredictability of the art, (6) the amount or

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direction or guidance presented, (7) the presence or absence of working examples, and (8) the quantity of experimentation necessary. Although the quantity of experimentation alone is not dispositive in a determination of whether the required experimentation is undue, this factor does play a central role. For example, a very limited quantity of experimentation may be undue in a fledgling art that is unpredictable where no guidance or working examples are provided in the specification and prior art, whereas the same amount of experimentation may not be undue when viewed in light of some guidance or a working example or the experimentation required is in a predictable established art. Conversely, a large quantity of experimentation would require a correspondingly greater quantum of guidance, predictability and skill in the art to overcome classification as undue experimentation. In *Wands*, the determination that undue experimentation was not required to make the claimed invention was based primarily on the nature of the art, and the probability that the required experimentation would result in successfully obtaining the claimed invention. (*Wands*, 8 USPQ2d 1406). Thus, a combination of factors which, when viewed together, would provide an artisan of ordinary skill in the art with an expectation of successfully obtaining the claimed invention with additional experimentation would preclude the classification of that experimentation as undue. A combination of *Wands* factors, which provide a very low likelihood of successfully obtaining the claimed invention with additional experimentation, however, would render the additional experimentation undue.

1.Breadth of the claims.

In regards to the product of the invention and the breadth of the claims the broadest interpretation that applies is to compounds presented by the general structure formula (I) of claim 1.

2. The nature of the invention.

The invention is a novel class of pharmaceutical compounds that are inhibitors of Hepatitis C Virus (HCV) protease activity, specifically macrocyclic compounds that inhibit HCV NS3/NS4a serine protease activity.

3. The state of prior art.

In regards to the macrocyclic compounds of the invention presented by the general structure formula (I) of claim 1, the prior art does not provide any evidence of HCV protease inhibitory activity- specifically with regards to HCV NS3/NS4a serine protease inhibitory activity.

4. The relative skill in the art.

The relative skill in the art as it relates to pharmaceutical macrocyclic compounds that inhibit the activity of HCV serine protease is that of a M.D. or Ph. D. level individual.

5. The level of predictability in the art.

Since the prior art does not teach that the compounds presented by general formula (I) of claim 1 formerly existed, the level of predictability is low in regards to the macrocyclic compounds of the invention with respect to HCV serine protease inhibitory activity. Therefore, one of skill in the art would not be able to readily anticipate the inhibitory effects of the macrocyclic compounds of the invention in view of HCV NS3/NS4a serine protease inhibitory activity.

6. The amount of guidance present.

The applicant has not provided guidance for all the compounds presented in the general formula (I) of claim 1. In table A of the specification of the present application, the applicant has provided results of a HCV protease continuous assay for a group of macrocyclic compounds wherein the applicant has categorized the K_i values associated with each investigated compound as a barometer of HCV serine protease inhibitory activity. If the K_i of a given compound is between 1-99nM then the compound is in category a, any value for a given compound that is above 100nM and below 999nM is considered to be in category b, if the K_i value is between 1000-9999nM the compound is considered to be in category c and if the K_i value is between 10,000-50,000 then the compound is considered to be in category d. The applicant has shown some guidance as to how certain macrocyclic compounds of the invention (table A, compounds 26 and 27, page 113) can be used to perhaps inhibit HCV protease activity - but the applicant has not provided guidance for all the compounds presented in the general structure formula (I) of claim 1 in regards to how they can be used to inhibit HCV serine protease activity.

7. The existence of working examples.

The specification, examples 19-23 (pages 92-105) provides specific working examples of macrocyclic compounds (table 1) that can be used to inhibit HCV serine protease activity. However, the specification does not provide working examples of all compounds suggested by the general structure formula (I) of claim 1.

8. The quantity of experimentation necessary.

In the case of using all the compounds suggested by the general structure formula (I) of claim 1, a large quantity of experimentation needs to be disclosed in order for a person skill in the art to be able to practice the invention, since there are a multitude of possible compounds that are suggested by the general structure formula of claim 1 and each compound needs to be tested for HCV protease inhibitory activity.

Due to the quantity of experimentation still required to be performed by one skill in the art in regards to how to use all the compounds suggested by the general formula (I) of claim 1, the lack of guidance presented in the specification regarding the same, the absence of a working example directed to same, the unpredictable nature of the invention with regards to HCV serine protease inhibitory activity, the state of the prior art not providing any evidence that all the compounds suggested by general formula (I) of claim 1 will exhibit HCV serine protease inhibitory activity , and the breath of the claims which fails to provide particular steps for all compounds suggested by the general formula (I) of claim 1 exhibiting HCV serine protease inhibitory activity, the specification fails to teach the skilled artisan in the art how to make and use the invention.

Claims 19-23 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 19 provides for the use of a pharmaceutical composition, but, since the claim does not set forth any steps involved in the method/process, it is unclear what

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method/process applicant is intending to encompass. A claim is indefinite where it merely recites a use without any active, positive steps delimiting how this use is actually practiced. **Claims 20-23** are dependent claims that do not further clarify the claim that they depend from.

In **claim 19** HCV needs to be spelled out in the first instant of use.

In **claim 22** the phrase still additionally is indefinite.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

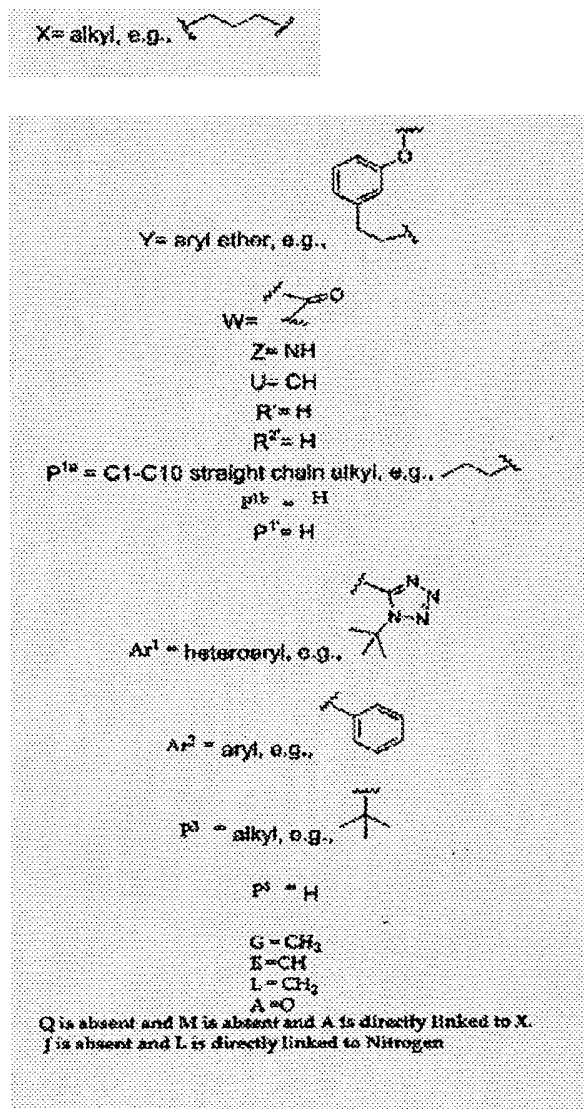
A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 19-23 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 1 of copending Application No. 09825399. Although the conflicting claims are not identical, they are not patentably distinct from each other because the general structural formula

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(I) of claim 1 of the present application provides for structures that fall within the scope of the possible structures provided by the general structural formula (I) of application 09825399 in view of the following moieties:



This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.


Conclusion

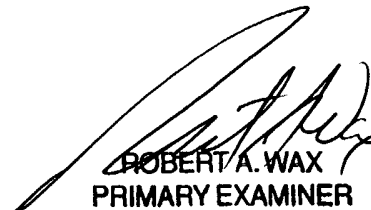
No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert B Mondesi whose telephone number is 571-272-0956. The examiner can normally be reached on 9am-5pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christopher Low can be reached on 571-272-0951. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).


Robert B Mondesi
Patent Examiner
Group 1653
04-12-04


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PRIMARY EXAMINER